

WHAT IS CLAIMED IS:

- 1 1. A crystal of a core RNA polymerase (RNAP) that effectively diffracts X-rays
2 for the determination of the atomic coordinates to a resolution of better than 3.5
3 Angstroms.
- 1 2. The crystal of Claim 1, wherein the core RNA polymerase is a bacterial core
2 RNA polymerase.
- 1 3. The crystal of Claim 2, wherein the bacterial core RNA polymerase is a
2 thermophilic bacterial core RNA polymerase.
- 1 4. The crystal of Claim 3, wherein the thermophilic bacterial core RNA
2 polymerase is a *Thermus aquaticus* bacterial core RNA polymerase.
- 1 5. The crystal of Claim 1, wherein the core RNA polymerase comprises a β'
2 subunit, a β subunit, and a pair of α subunits.
- 1 6. The crystal of Claim 5, further comprising an ω subunit.
- 1 7. The crystal of Claim 1 that effectively diffracts X-rays for the determination
2 of the atomic coordinates of the core RNA polymerase to a resolution of 3.3
3 Angstroms or better.
- 1 8. The crystal of Claim 7 having space group of $P4_12_12$ and a unit cell of
2 dimensions of $a = b = 201$ and $c = 294 \text{ \AA}$.
- 1 9. A method of identifying an agent for use as an inhibitor of bacterial RNA
2 polymerase using the crystal of Claim 1 or a dataset comprising the three-
3 dimensional coordinates obtained from the crystal, comprising:

- 4 (a) selecting a potential agent by performing rational drug design with
5 the three-dimensional coordinates determined from the crystal, wherein said
6 selecting is performed in conjunction with computer modeling;
- 7 (b) contacting the potential agent with the bacterial RNA polymerase;
8 and
- 9 (c) measuring the activity of the bacterial RNA polymerase; wherein a
10 potential agent is identified as an agent that inhibits bacterial RNA polymerase when
11 there is a decrease in the activity of the bacterial RNA polymerase.

1 10. The method of Claim 9, further comprising:

- 2 (d) growing a supplemental crystal containing the core RNA polymerase
3 formed in the presence of the potential agent, wherein the crystal effectively
4 diffracts X-rays for the determination of the atomic coordinates to a resolution of
5 better than 5.0 Angstroms;
- 6 (e) determining the three-dimensional coordinates of the supplemental
7 crystal with molecular replacement analysis; and
- 8 (f) selecting a second generation agent by performing rational drug
9 design with the three-dimensional coordinates determined for the supplemental
10 crystal, wherein said selecting is performed in conjunction with computer modeling.

1 11. The method of Claim 10, further comprising:

- 2 (g) contacting the second generation agent with a eukaryotic RNA
3 polymerase; and
- 4 (h) measuring the activity of the eukaryotic RNA polymerase; wherein a
5 potential agent is identified as an agent for use as an inhibitor of bacterial RNA
6 polymerase when there is no change in the activity of the eukaryotic agent RNA
7 polymerase.

1 12. A method of identifying an agent that inhibits bacterial growth using the
2 crystal of Claim 1, or a dataset comprising the three-dimensional coordinates
3 obtained from the crystal, comprising:
4 (a) selecting a potential agent by performing rational drug design with
5 the three-dimensional coordinates determined for the crystal, wherein said selecting
6 is performed in conjunction with computer modeling;
7 (b) contacting the potential agent with a bacterial culture; and
8 (c) measuring the growth of the bacterial culture, wherein a potential
9 agent is identified as an agent that inhibits bacterial growth when there is a decrease
10 in the growth of the bacterial culture.

1 13. The method of Claim 12, further comprising:
2 (d) growing a supplemental crystal containing the core RNA polymerase
3 formed in the presence of the potential agent, wherein the crystal effectively
4 diffracts X-rays for the determination of the atomic coordinates to a resolution of
5 better than 5.0 Angstroms;
6 (e) determining the three-dimensional coordinates of the supplemental
7 crystal with molecular replacement analysis; and
8 (f) selecting a second generation agent by performing rational drug
9 design with the three-dimensional coordinates determined for the supplemental
10 crystal, wherein said selecting is performed in conjunction with computer modeling.

1 14. The method of Claim 13, further comprising:
2 (g) contacting the second generation agent with a eukaryotic cell; and
3 (h) measuring the amount of proliferation of the eukaryotic cell; wherein
4 a potential agent is identified as an agent for inhibiting bacterial growth when there
5 is no change in the proliferation of the eukaryotic cell.

1 15. A method of identifying an agent for use as an inhibitor of bacterial RNA
2 polymerase using the three-dimensional coordinates for the *Thermus aquaticus* core
3 RNA polymerase comprising:

4 (a) selecting a potential agent by performing rational drug design with
5 the three-dimensional coordinates determined for the *Thermus aquaticus* core RNA
6 polymerase, wherein said selecting is performed in conjunction with computer
7 modeling;

8 (b) contacting the potential agent with the bacterial RNA polymerase;
9 and

10 (c) measuring the activity of the bacterial RNA polymerase; wherein a
11 potential agent is identified as an agent that inhibits bacterial RNA polymerase when
12 there is a decrease in the activity of the bacterial RNA polymerase.

1 16. The method of Claim 15, further comprising:

2 (d) growing a crystal containing a bacterial RNA polymerase formed in
3 the presence of the potential agent, wherein the crystal effectively diffracts X-rays
4 for the determination of the atomic coordinates to a resolution of better than 5.0
5 Angstroms;

6 (e) determining the three-dimensional coordinates of the crystal with
7 molecular replacement analysis; and

8 (f) selecting a second generation agent by performing rational drug
9 design with the three-dimensional coordinates determined for the crystal, wherein
10 said selecting is performed in conjunction with computer modeling.

1 17. The method of Claim 16, further comprising:

2 (g) contacting the second generation agent with a eukaryotic RNA
3 polymerase; and

4 (h) measuring the activity of the eukaryotic RNA polymerase; wherein a
5 potential agent is identified as an agent for use as an inhibitor of bacterial RNA

6 polymerase when there is no change in the activity of the eukaryotic agent RNA
7 polymerase.

1 18. A method of identifying an agent that inhibits bacterial growth using the
2 three-dimensional coordinates obtained for the *Thermus aquaticus* core RNA
3 polymerase, comprising:

4 (a) selecting a potential agent by performing rational drug design with
5 the three-dimensional coordinates determined for the *Thermus aquaticus* core RNA
6 polymerase, wherein said selecting is performed in conjunction with computer
7 modeling;

8 (b) contacting the potential agent with a bacterial culture; and

9 (c) measuring the growth of the bacterial culture; wherein a potential
10 agent is identified as an agent that inhibits bacterial growth when there is a decrease
11 in the growth of the bacterial culture.

1 19. The method of Claim 18 further comprising:

2 (d) growing a crystal containing a bacterial RNA polymerase formed in
3 the presence of the potential agent, wherein the crystal effectively diffracts X-rays
4 for the determination of the atomic coordinates to a resolution of better than 5.0
5 Angstroms;

6 (e) determining the three-dimensional coordinates of the crystal with
7 molecular replacement analysis; and

8 (f) selecting a second generation agent by performing rational drug
9 design with the three-dimensional coordinates determined for the crystal, wherein
10 said selecting is performed in conjunction with computer modeling.

1 20. The method of Claim 19, further comprising:

2 (g) contacting the second generation agent with a eukaryotic cell; and

- 3 (h) measuring the amount of proliferation of the eukaryotic cell; wherein
4 a potential agent is identified as an agent for inhibiting bacterial growth when there
5 is no change in the proliferation of the eukaryotic cell.

1 21. A method of obtaining a crystal of a core bacterial RNA polymerase
2 comprising growing a core bacterial RNA polymerase crystal in a buffered solution
3 containing 40-45% saturated ammonium sulfate.

1 22. The method of Claim 21 wherein said growing is performed by a method
2 selected from the group consisting of batch crystallization, vapor diffusion, and
3 microdialysis.